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EXAMINER

LU, FRANK WEI MIN

ART UNIT	PAPER NUMBER
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1634

NOTIFICATION DATE	DELIVERY MODE
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02/06/2009

ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No. 10/796,298	Applicant(s) MITSUHASHI, MASATO	
	Examiner FRANK W. LU	Art Unit 1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 26 November 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 73,75,77-93,215 and 217-239 is/are pending in the application.
- 4a) Of the above claim(s) 89,90,220-230 and 234-237 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 73,75,77-88,91-93,215,217-219,231-233,238 and 239 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 13 February 2006 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>1/14/2009</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

CONTINUED EXAMINATION UNDER 37 CFR 1.114 AFTER FINAL REJECTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission of RCE and the amendment filed on November 26, 2008 have been entered. The claims pending in this application are claims 73, 75, 77-93, 215, and 217-239 wherein claims 89, 90, 220-230, and 234-237 have been withdrawn due to species election and election by original presentation. Rejection and/or objection not reiterated from the previous office action are hereby withdrawn in view of applicant's amendment filed on November 26, 2008. Claims 73, 75, 77-88, 91-93, 215, 217-219, 231-233, 238, and 239 will be examined.

Claim Objections

2. Claim 73 is objected to because of the following informalities: (1) "the blood sample" in step (d) should be "the whole blood"; (2) "sample mRNA and spiked control RNA" in line 2 of step (f) should be "the sample mRNA and the spiked control RNA"; (3) "spiked control RNA" in steps (g) and (h) should be "said spiked control RNA"; and (4) "sample mRNA" in step (h) should be "said sample mRNA".
3. Claim 91 is objected to because of the following informality: "cDNA" should be "the cDNA".

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4. Claim 215 is objected to because of the following informality: “oligo(dT)” in lines 4 and 7 of step (g) should be “said oligo(dT)”.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. New Matter

Claims 73, 75, 77-88, 91-93, 231-233, 238, and 239 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

First, the recitation “said spiked control RNA is non-homologous to RNA from the blood sample” is added to newly amended dependent claim 73. However, the specification fails to define or provide any disclosure to support such claim recitation in claim 73. Second, the recitation “test the side effects of anti-leukemia drugs that induce specific mRNA responsible for apoptosis development in leukocytes” is added to newly dependent claim 233. Although the specification describes to test the side effects of anti-cancer drugs on white blood cells (see original filed claim 29) and describes that the genes related to apoptosis are candidate genes for anti-leukemia drugs (see Table 1 in page 8), the specification fails to define or provide any disclosure to support such claim recitation in claim 233 because anti-cancer drugs recited in

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original filed claim 29 is not limited to anti-leukemia drugs and may include other drugs which are not anti-leukemia drugs and apoptosis candidate genes of anti-leukemia drugs disclosed by the specification are not limited to apoptosis candidate genes of leukocytes and may include other apoptosis candidate genes which are not found in leukocytes. Third, the recitation “the whole blood is exposed to donor cells prior to filtration” is added to the newly dependent claim 238 while the recitation “the quantification of a higher than normal level of the mRNA is indicative of transplant rejection” is added to the newly dependent claim 239. Although the specification describes that the mRNA of donor cell-mediated cytokines is quantified wherein the quantification of mRNA of donor cell-mediated cytokines is used to test transplant rejection (see original filed claims 34 and 35), the specification fails to define or provide any disclosure to support such claim recitations in claims 238 and 239. Fourth, the specification also does not describe that a plurality of different antisense primers for different specific mRNAs are present in the lysis buffer as recited in claim 217. Fifth, in applicant’s remarks filed on November 26, 2008, applicant does not indicate which parts in the specification supports such claim recitations recited in claims 73, 217, 233, 238, and 239.

MPEP 2163.06 notes “IF NEW MATTER IS ADDED TO THE CLAIMS, THE EXAMINER SHOULD REJECT THE CLAIMS UNDER 35 U.S.C. 112, FIRST PARAGRAPH - WRITTEN DESCRIPTION REQUIREMENT. *IN RE RASMUSSEN*, 650 F.2D 1212, 211 USPQ 323 (CCPA 1981).” MPEP 2163.02 teaches that “Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed...If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application.” MPEP 2163.06 further notes “WHEN AN AMENDMENT IS FILED IN REPLY TO AN OBJECTION OR REJECTION BASED ON 35 U.S.C. 112, FIRST PARAGRAPH, A STUDY OF THE ENTIRE APPLICATION IS OFTEN NECESSARY TO DETERMINE WHETHER OR NOT “NEW MATTER” IS INVOLVED. *APPLICANT SHOULD THEREFORE SPECIFICALLY POINT OUT THE SUPPORT FOR ANY AMENDMENTS MADE TO THE DISCLOSURE*” (emphasis added).

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7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 73, 75, 77-88, 91-93, 215, 217-219, 231-233, 238, and 239 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

9. Claim 73 recites the limitation “the sample mRNA” in step (f) of the claim. There is insufficient antecedent basis for this limitation in the claim because there is no phrase “sample mRNA” in steps (a) to (e). Please clarify.

10. Claim 73 is rejected as vague and indefinite in view of step (h) because it is unclear that mRNA in step (h) is the target mRNA in the preamble or not. Please clarify.

11. Claim 77 is rejected as vague and indefinite. Since there is no method step for collection of leukocytes in claim 73, it is unclear why heparin is administered to the whole blood prior to collection of leukocytes. Please clarify.

12. Claim 78 is rejected as vague and indefinite. Since there is no filtration step in claim 73, it is unclear why the whole blood is frozen and subsequently thawed prior to filtration. Please clarify.

13. Claim 80 or 81 is rejected as vague and indefinite. Since the phrase “each filter plate” in claim 80 or 81 means two or more filter plates while claim 79 only requires one multi-well filter plate, claim 79 and claim 80 or 81 do not correspond each other. Please clarify.

14. Claim 83 is rejected as vague and indefinite. Since claim 75 only requires one filter membrane while claim 83 requires a plurality of filter membranes, claims 75 and 83 do not correspond each other. Please clarify.

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15. Claim 88 is rejected as vague and indefinite because centrifugation is not considered as a transfer step. Please clarify.

16. Claim 91 is rejected as vague and indefinite because it is unclear that mRNA is the sample mRNA or not. Please clarify.

17. Claim 91 recites the limitation “the specific mRNA” in the claim. There is insufficient antecedent basis for this limitation in the claim because there is no phrase “specific mRNA” in claim 73. Please clarify.

18. Claim 92 or 93 is rejected as vague and indefinite because it is unclear that specific antisense primers is applied to where. Please clarify.

19. Claim 215 is rejected as vague and indefinite in view of steps (g) and (h). Since the solution in step (g) does not contain the specific mRNA but contains the cDNA formed by extension of the antisense primer, it is unclear why the specific mRNA can be from said cDNA solution as recited in step (h). Please clarify.

20. Claim 215 is rejected as vague and indefinite in view of step (g) because it is unclear that the primers in step (g) is identical to antisense primers in step (d) or not. Furthermore, the phrase “the cDNA formed by extension of the antisense primers goes into solution as a result of displacement by the cDNA formed by extension of oligo(dT) without heat denaturation” does not make sense. Does this phrase mean that the cDNA formed by extension of the antisense primers goes into solution as a result of displacement by the cDNA formed by extension of said oligo(dT) without heat denaturation of said specific mRNA and the cDNA formed by extension of the antisense primer? Please clarify.

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21. Claim 218 is rejected as vague and indefinite because it is unclear that the cDNA in the claim means the cDNA formed by extension of oligo(dT) or the cDNA formed by extension of the antisense primer or both the cDNA formed by extension of oligo(dT) and the cDNA formed by extension of the antisense primer. Please clarify.

22. Claim 231 is rejected as vague and indefinite. Since claim 73 does not indicate that the target mRNA is the mRNA of apoptosis genes, it is unclear why the mRNA of apoptosis genes can be quantified. Please clarify.

23. Claim 231 recites the limitation “the mRNA of apoptosis genes” in the claim. There is insufficient antecedent basis for this limitation in the claim because there is no mRNA of apoptosis genes in claim 73. Please clarify.

24. Claim 232 is rejected as vague and indefinite. Since claim 73 does not indicate that the target mRNA is the mRNA of cytokines, it is unclear why the mRNA of cytokines can be quantified. Please clarify.

25. Claim 232 recites the limitation “the mRNA of cytokines” in the claim. There is insufficient antecedent basis for this limitation in the claim because there is no mRNA of cytokines in claim 73. Please clarify.

26. Claim 233 is rejected as vague and indefinite. Since claim 73 does not indicate that the target mRNA is a specific mRNA responsible for apoptosis development in leukocytes, it is unclear why the quantification of mRNA can be used to test the side effects of anti-leukemia drugs that induce mRNA responsible for apoptosis development in leukocytes. Please clarify.

27. Claim 238 is rejected as vague and indefinite. Since claim 73 does not have a filtration step, it is unclear why the whole blood is exposed to donor cells prior to filtration. Please clarify.

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28. Claim 239 is rejected as vague and indefinite. Since claim 73 does not indicate that the target mRNA is related to transplant rejection, it is unclear why the quantification of a higher than normal level of the mRNA can be indicative of transplant rejection. Please clarify.

Conclusion

29. No claim is allowed.

30. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is (571)273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (571)272-0746. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached on (571)272-0735.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

/Frank W Lu /
Primary Examiner, Art Unit 1634
February 2 2009